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10/588,792	10/26/2006	Hiroyuki Kamiya	2006_1315A	9531

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EXAMINER	
PANDE, SUCHIRA	
ART UNIT	**PAPER NUMBER**
1637	

NOTIFICATION DATE	DELIVERY MODE
04/09/2012	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/588,792	KAMIYA ET AL.	
	Examiner	Art Unit	
	SUCHIRA PANDE	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2012*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *12,13 and 15-23* is/are pending in the application.

5a) Of the above claim(s) *17-22* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *12, 13,15-16 and 23* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment filed on 3/13/2012 is acknowledged. Applicant has amended base claim 12. Claims 17-22 remain withdrawn. Claims 12-13, 15-16 and 23 are active and will be examined in this action.

Response to arguments

Re 112 Rejections of claims 12-13, 15-16 and 23

2. Applicant has amended claim 12 to add limitation ---"wherein the target DNA is double-stranded DNA and the target DNA sense strand encodes a protein." Addition of this limitation obviates the 112 1st written description, scope of enablement rejection as well as 112 2nd indefiniteness rejection of claims 12-13, 15-16 and 23.

Re 102 rejection of claims 12-13, 16 and 23 over Bilang et al.

3. Applicant's arguments filed 3/13/2012 have been fully considered but they are not persuasive. Base claim 12 has been amended to add the limitation –"-wherein the target DNA is double-stranded DNA and the target DNA sense strand encodes a protein".

This newly added limitation is taught by Bilang et al.

See Fig. 4 on page 333 where homologous recombination between pBSKB1 ds (double-stranded plasmid containing hph target is taught) and pTZR3ss PvuII-EcoRI linear fragment (single-stranded fragment) is shown. See page 332 col. 2 first full par. where transformation with either coding or non coding strand of marker gene is taught. Thus by teaching coding strand of hygromycin phospho- transferase enzyme (hph gene), Bilang teaches the target DNA sense strand encodes a protein. Fig. 4 shows a

base conversion is observed by using ds DNA target present in plasmid and **ss** DNA fragment.

Hence 102 rejection of claims 12-13, 16 and 23 over Bilang et al. are applicable to amended claims, hence are being maintained. Applicant's arguments regarding superior efficiency are not sufficient to overcome 102 rejection. Arguments regarding superior results can be used to overcome a 103 obviousness rejection not an anticipatory 102 rejection.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 12, 13, 16 and 23 rejected under 35 U.S.C. 102(b) as being anticipated by Bilang et al. (1992) Molecular and Cellular Biology vol. 12 no.1 pp 329-336 (previusly cited) as evidenced by Genbank accession no JA136868 which shows the hygromycin resisitance gene (hph) is 1026 bp long (previously cited)

Regarding claim 12, Bilang et al. teach: homologous recombination in *Nicotiana tabacum* (see abstract lines 2-3), by teaching homologous recombination, Bilang et al. teaches an in vitro base conversion method of a DNA sequence (see claim interpretation above),

which is a method of converting one or more bases in a target DNA sequence in a cell (see page 332 fig. 2 legend where hph-encoding gene is taught as target DNA sequence that is converted by homologous recombination) in a cell (*Nicotiana tabacum* is taught as the cell)),

consisting of preparing a single-stranded DNA fragment having 300 to 3,000 bases by cleavage from a single- stranded circular DNA (see page 330 section plasmid DNA where site-directed linearization of ssDNA circular DNA is taught. See Table 1 where oligos used for site directed cleavage of ss recombinant substrates obtained from using pBluescript vectors is taught. See Fig. 2 and legend where hph gene is shown cloned under control of CaMV35S promoter followed by polyadenylation site in constructs pTZR1 and pTZR2 that use phage replication starting at M13 inter genic region (f1) resulting in excretion of the coding i.e. complementary to mRNA, strand of hph. The full length open reading frame of hph gene is 1026 bp (see Genbank sequence accession no JA136868). Non overlapping deletion derivatives of this full length hph gene are used for homologous recombination, hence prior art teaches use of constructs that express full length single stranded circular DNA containing 1026 base long hph DNA or shorter deletion sequences. Thus cited art teaches use of 1026 or shorter hph sequences expressed as SS circular DNA, as starting point which is then linearized using oligos recited in Table 1. Since 1026 and shorter sequences fall within the range of 300 to 3,000 bases, cited art anticipates the recited limitation namely preparing a single-stranded DNA fragment having 300 to 3,000 bases by cleavage from a single- stranded circular DNA), and

introducing said single-stranded DNA fragment into a cell (see page 329 last par. where transformation of protoplasts using ssDNA is taught. Also see page 331 Fig. 1 where result of homologous recombination performed are tabulated. Lines B of each co transformation experiment is performed with linear is shown, thus teaching introducing said single-stranded DNA fragment into a cell)

wherein said single-stranded DNA fragment is homologous with a sense strand of the target DNA sequence and contains the base(s) to be converted (see fig. 2 legend where pTZR1 construct is taught to excrete coding strand i.e. complementary to mRNA of hph gene while pTZR2 is taught to excrete the non coding strand of hph, also see page 332 full par. 3 where The recombination frequencies of ss substrate of the same polarity (unable to anneal, class 1) were rather low and the relative recombination frequencies obtained with substrates defined as class 2 (complementary and thus could anneal directly) were high—the class 2 single stranded DNA fragment of prior art corresponds to the said single-stranded DNA fragment is homologous with a sense strand of the target DNA sequence of instant claim, and contains the region of gene to be converted,

wherein the target DNA is double stranded DNA and the target DNA sense strand encodes a protein. (See Fig. 4 on page 333 where homologous recombination between pBSKB1 ds (double-stranded plasmid containing hph target is taught) and pTZR3ss PvuII-EcoRI linear fragment (single-stranded fragment) is shown. See page 332 col. 2 first full par. where transformation with either coding or non coding strand of marker gene is taught. Thus by teaching coding strand of hygromycin phospho-

transferase enzyme (hph gene), Bilang teaches Fig. 4 shows a base conversion is observed by using ds DNA target present in plasmid and **ss** DNA fragment wherein the target DNA is double stranded DNA and the target DNA sense strand encodes a protein) thus teaching all the limitations of base claim 12.

Regarding claim 13, Bilang et al. teaches wherein the single-stranded circular DNA is a phagemid DNA (pTZR1 and pTZR2 see fig. 2A legend are phagemids).

Regarding claim 16, Bilang et al. teaches wherein one or more bases in a target DNA sequence in a cell of an organism are converted (see page 331 section assay for stably integrated products of intermolecular homologous recombination between ssDNA molecules and Fig. 1 panel 1 B).

Regarding claim 23, Bilang et al. teaches the target gene is present in the extruded or excreted phage DNA (extruded or excreted DNA corresponds to genomic DNA of phage f1), thereby teaching wherein the target gene is genomic DNA.

Thus Bilang et al. anticipate the subject matter recited in claims 12, 13, 16 and 23.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 15 rejected under 35 U.S.C. 103(a) as being unpatentable over Bilang et al. as applied to claim 12 above, and further in view of Zarling et al. (US PG PUB 2004/0019916 A1 with priority back to 1997—previously cited).

Regarding claim 15, Bilang et al. teaches method of claim 12 above, but do not teach wherein the target DNA sequence in the cell is a DNA sequence causing a disease due to the one or more bases.

Regarding claim 15, Zarling et al. teaches wherein the target DNA sequence in the cell is a DNA sequence causing a disease due to the one or more bases (see page 16 par. 0131 where target DNA associated with CFTR gene is taught. CFTR is associated with human disease cystic fibrosis. See page 19 par. 0150 where CFTR genomic DNA containing a 3bp ΔF508 deletion is taught as the target that causes disease).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use any desired double stranded DNA of interest that may be derived from genomic DNA such as the CFTR genomic DNA containing a 3bp ΔF508 deletion taught by Zarling et al. as the starting target DNA sequence that is to be converted.

The 3bp ΔF508 deletion in CFTR gene results in formation of a defective transmembrane protein which results in Cystic Fibrosis disease that is highly prevalent in Caucasian population. One of ordinary skill in the art has a reasonable expectation that they would be able to convert the 3bp ΔF508 deletion to the corresponding wild type in the target cell using the method of Bilang et al. Hence one of ordinary skill in the art would be motivated to use the DNA sequence causing a disease as taught by Zarling et al. as the target and perform the in vitro base conversion method of Bilang et al. on this starting DNA with a reasonable expectation of success in being able to correct the genetic aberration by restoring the corresponding wild type form of the targeted sequence.

Conclusion

9. Claims 12-13, 15-16 and 23 remain rejected.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUCHIRA PANDE whose telephone number is (571)272-9052. The examiner can normally be reached on 6:30 am -3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

/TERESA E STRZELECKA/
Primary Examiner, Art Unit 1637
April 3, 2012